



Breakthrough Innovations for better and healthier Crops

“KeyGene’s views for the future”

Arjen J van Tunen, CEO KeyGene

Crop Innovation & Business 2019

KeyGene

the Crop Innovation Company

*1989; Visionary group of breeders,
embracing the opportunity of biotech*



*1989 – 2019;
From Technology & Trait Provider to
Crop Innovation Company*



*“Our **Innovation Platforms** work in harmony
to provide integrated solutions
for current and future crop challenges”*

Our World of Today

Our ever changing world: what is happening?

Major developments:

- China, India economies: economic growth slows down; growth in 2019 in Europe 1.3 %; NL with 1.9% still fine
- Impact of trade wars
- Enormous consolidations in the industry to big 4 that now all combine seeds, agro chemicals and GM: 1. Bayer (with Monsanto), 2. Corteva (Ag Dow & Ag Dupont), 3. Syngenta / Chinachem, 4. BASF
- New competition: nice varieties developed by many requires transformational new varieties from the leading seed companies which make a difference in the market
- Major VC investments in Agri domain (e.g. USA)
Need now to monetize investments



Our World of Today

Our ever changing world: what is happening?

Major developments:

- **Need** for more, healthy and better food e.g. via fruits and vegetables
- **Need** for sustainable agricultural production
- **Need** to adapt to climate change
- **Need** for data management, AI and Machine learning at all levels through the food demand chain. New entrants like MicroSoft, Amazon Web Services and IBM
- **Need** for more and new forms of alliances and collaborations

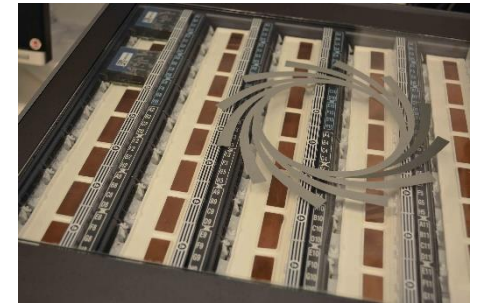


Requires the development of:
Breakthrough Technologies, Better Traits & New and Improved Crops

Breakthrough Technologies

Genomics & Phenomics

- **Mainstream Farming:** using varieties developed via crossing and selection supported by DNA technologies and Genomics
Large track record of good quality products developed sold for acceptable price
- **Large-scale Farming:** using varieties developed via GM, Gene Editing & Big Data: corn, soybean, canola, cotton, sugar beet at multinationals
Large scale, cost effective for farmer, data-driven, innovative, risk perception often high (esp. in EU, Japan and for Food also in China and India)
- **Organic Farming:** using varieties developed via traditional crossing and selection, no GM, Genomics and MAB ok, no chemicals, low yields
Currently niche activities but growing
- **New: Vertical Farming:** production in multiple layers in factories in our cities or at home. Leafy vegetables & herbs first. New adapted varieties wanted
I strongly embrace this because of food safety & sustainability & local production aspects. But: maybe too technical?



Better Traits

Interesting “old” and new traits

- Yield & Yield Stability (feed the world, revolution in photosynthesis)
- Abiotic Stress Tolerance (adapt our crops to climate change)
- Biotic Stress Resistances (sustainability, reduce the use of agro chemicals)
- Quality, Taste (to serve more middle class consumers)
- Long shelf life (stop reducing waste!)
- Health (longer, better life for all of us)

*Besides some new traits,
many “old” traits are still of high interest*



New and Improved Crops

Genomics and Phenomics enables innovations in all crops

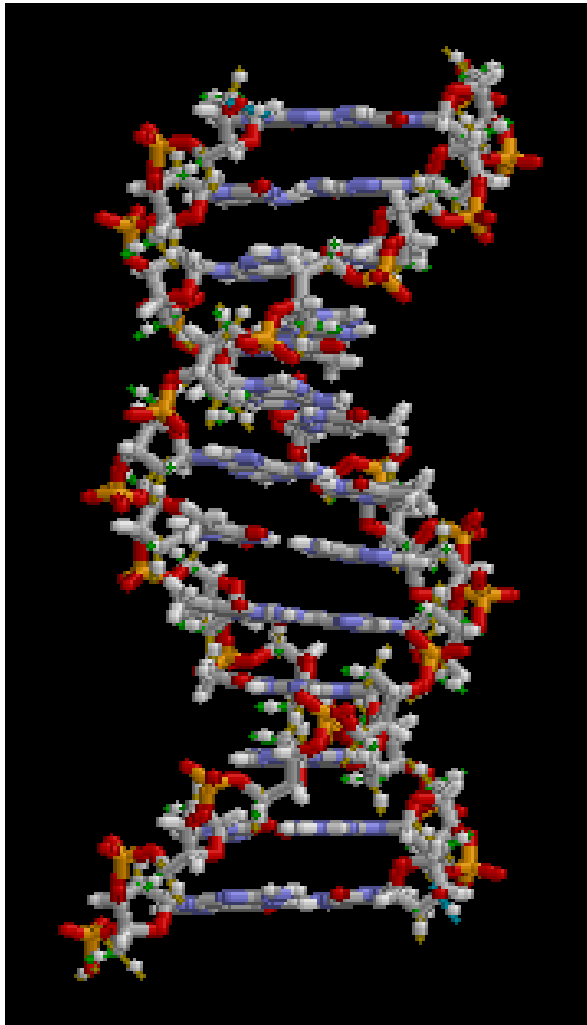
- **Accelerate** improvement of current cash crops (e.g. corn, soybean, tomato, lettuce)
- **Increase** improvement of small crops (e.g. ornamentals, berries)
- **Start** improvement of plantation crops (e.g. oil palm, banana)
- **Start** improvement of difficult and polyploidy crops (e.g. onion, potato, wheat, strawberry)
- **Enable** improvement of orphan & vegetatively propagated crops (e.g. cassava, millet, plantain, trees)
- **Domesticate** and develop new crops (e.g. dandelion for rubber, stevia for sweetener)



Because of cost reductions and high throughput & specificity in genomics and phenomics we can now molecularly improve crops that we could not touch before

DNA: source of genetic information

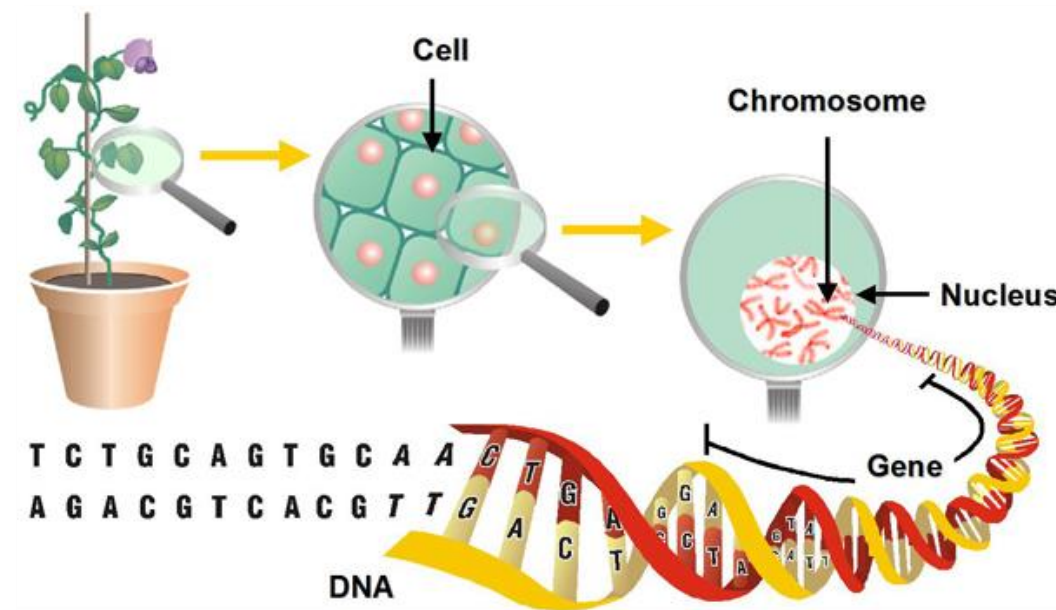
DNA the basis for breeding: since 1953



DNA has 4 building blocks (GATC)

Not digital but quatro-code

In all plant cells



DNA: source of genetic information

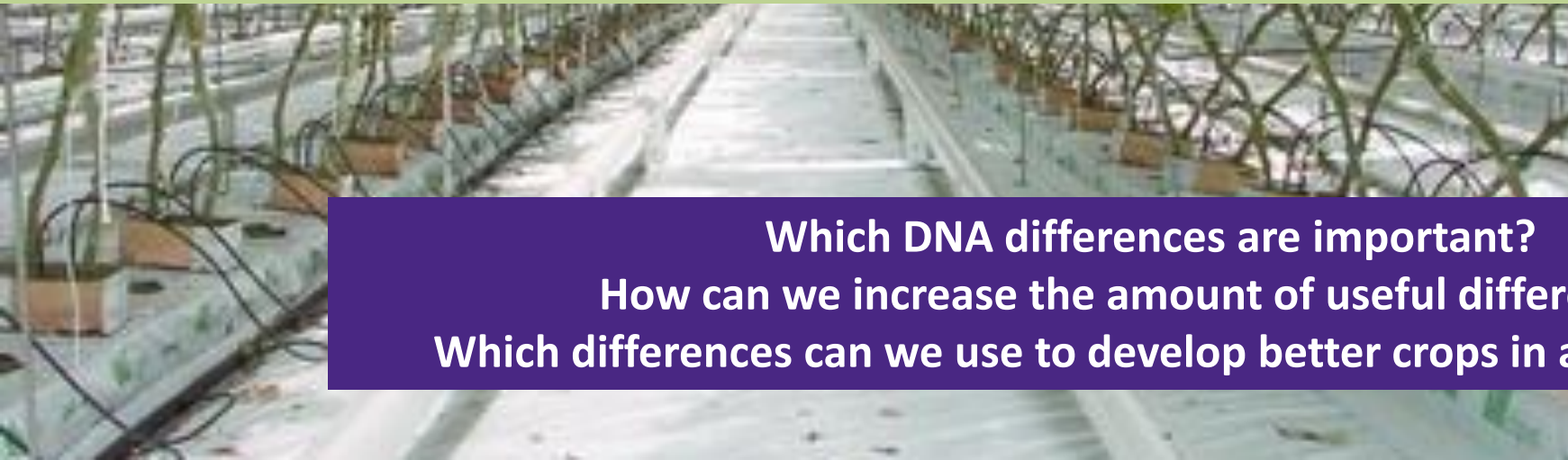
DNA from each crop plant differs = genetic variation!



Tomato DNA consists of 1.000.000.000 code letters (human: 3 x more)
 In DNA of 2 different commercial tomato plants: ~ 500.000 differences
 With a third plant: ~ 800.000 differences
 In 100 different commercial tomato varieties: ~ 10 million differences
 Between commercial and wild tomato species: ~ 100 million differences



Molecular Plant Breeding

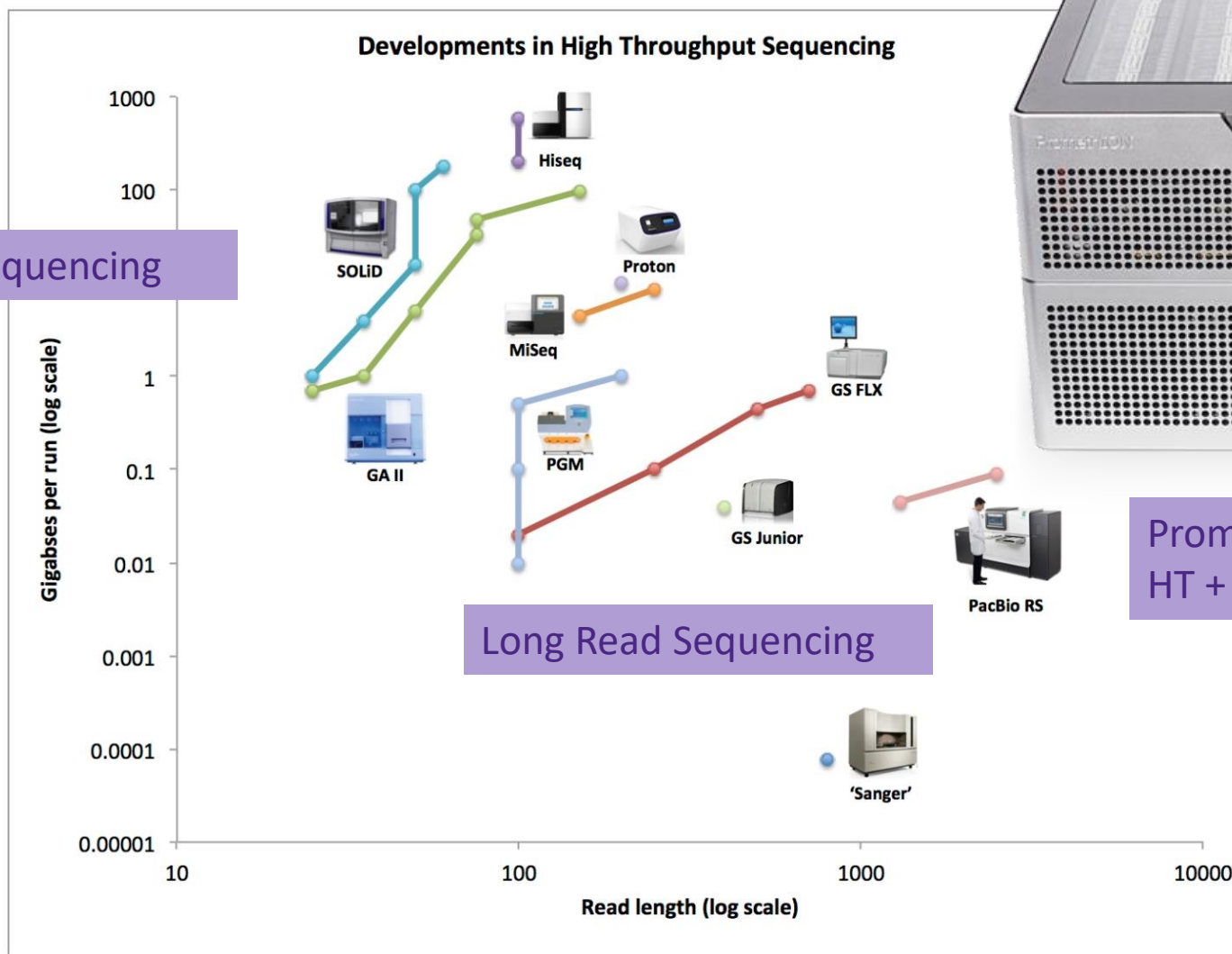


Which DNA differences are important?
 How can we increase the amount of useful differences?
 Which differences can we use to develop better crops in a non GM way?

Breakthrough Technologies

Paradigm shifts in sequencing: Cost ↓ Quality ↑

HT Short Read Sequencing



PromethION
HT + Long Read Sequencing



Breakthrough Technologies

The genome challenges in crops

Plant genomes can be **large**

- From 100 Mbp to 150 Gbps

Plant genomes can be **complex**

- Repeats
- Heterozygosity
- Polyploidy
- Large variation



Melon
2n ~0.4 Gb
low-copy DNA
The Tomato Genome Consortium (2012) Nature 485: 63
5 – 641



Pepper
2n ~3.5 Gb
~81% repetitive sequences
Qin et al. (2014) PNAS 111: 5135-5140



Cotton
4n ~2.3Gb
~69% repetitive sequences
Li et al. (2014) Nature Gen. 46: 567 – 572



Common Wheat
6n ~17 Gb
~80% repetitive sequences
Brenchley et al. (2012) Nature 491: 705 – 710.



Onion
2n 16 Gb
Currently sequencing

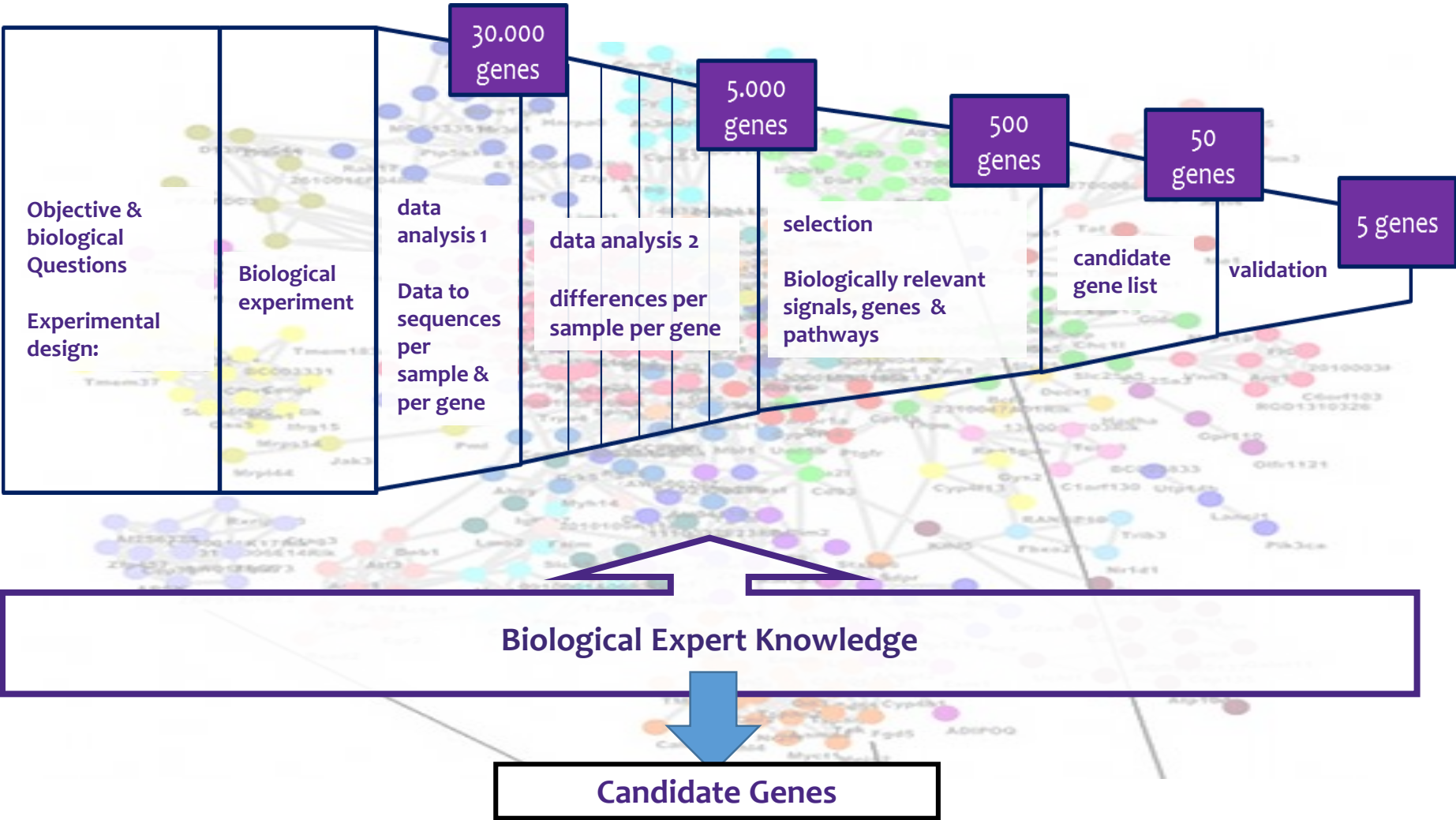


Tomato
2n ~0.9 Gb
low-copy DNA
The Tomato Genome Consortium (2012) Nature 485: 63
5 – 641

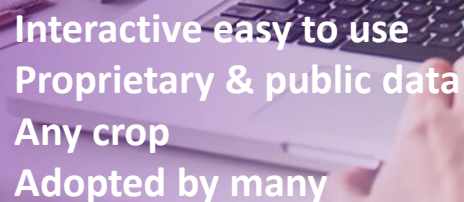


Trait Discovery - KeySeeQ[®]

Transcriptomics based discovery

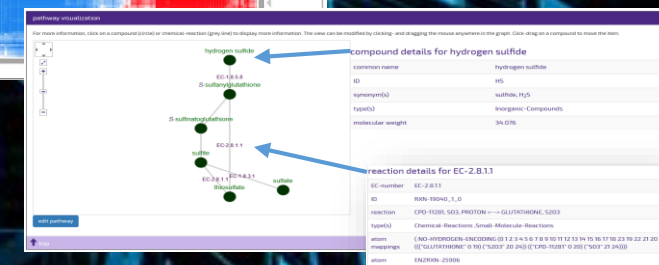


Powerful data analysis & visualization platform



- [illegible]

Bio-informatician Top 5 Global breeding company



Breakthrough Technologies

KeyPoint® Breeding

Mutagenesis



+

Chemical Mutagen
(eg EMS)



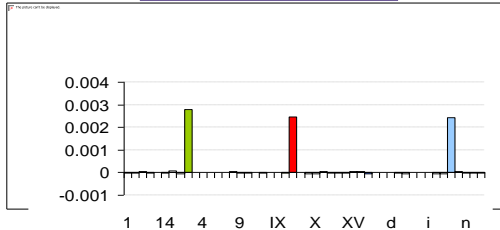
Grow Mutagenized Population



Isolate DNA
Pool DNA
Screen for mutation
In your genes of interest



Targeted detection
novel variants



Selection & verification of novel variant plants



GENOTYPE & PHENOTYPE
Pre-breeding material
with mutation in your
Gene of interest

KeyPoint® Breeding

KeyGene's Sequence Based, non GM Mutation Detection System



For many Crops:

Vegetables

Tomato, Sweet & Hot Pepper, Cabbage, Cucumber, Melon

Field Crops

Potato, Rye, Wheat, Sugar Beet, Tobacco, Dandelion, Soybean, Corn, Canola, Sorghum, Rice, Barley, Cassava, Sunflower

Flowers

Ornamental Sunflower

In-house industrialized procedure in one run:

- 4.000 – 25.000 mutagenized plants
- up to 20 genes simultaneously screened
- non-GM with patentable mutations
- combined with KeySeeQ® gene discovery system
- linked to strong allele selection prediction
- many mutants phenotyped in KeyGene's robotized and automated phenotyping system: **PhenoFab®**

Breakthrough Technologies

PhenoFab[®] Phenotyping

Applications:

- phenotype hundreds of KeyPoint mutants
- characterize biologicals
- characterize growth substances
- assay root nematode resistances
- ... and many others



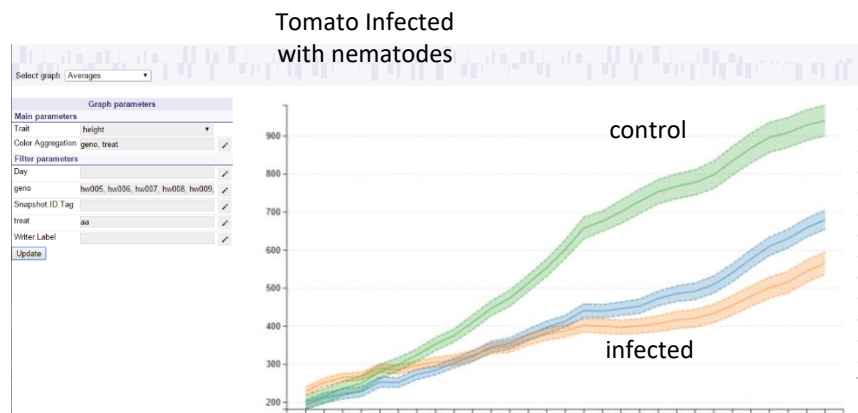
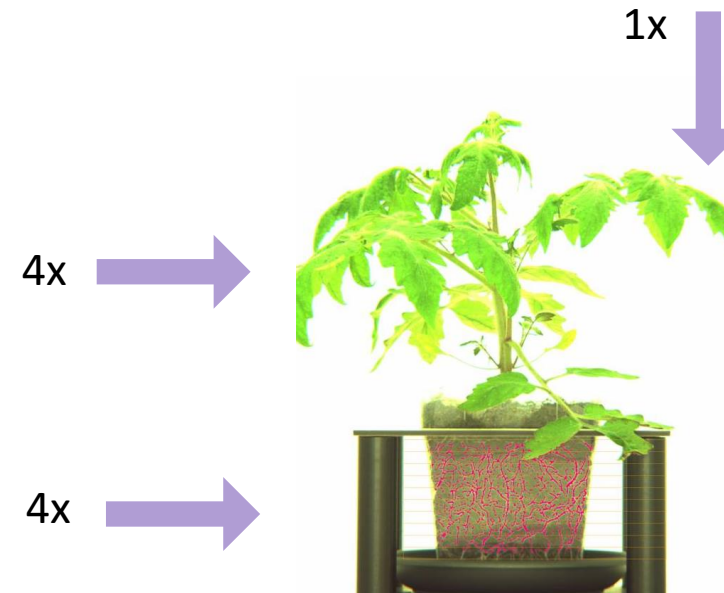
PhenoFab[®] Data management

Data Management:

- 400 plants x 9 pictures / plant x 35 days
= 126.000 digital images!

Deploy:

- Interactive data mining in PhenoReport
- VR Breeding Tool

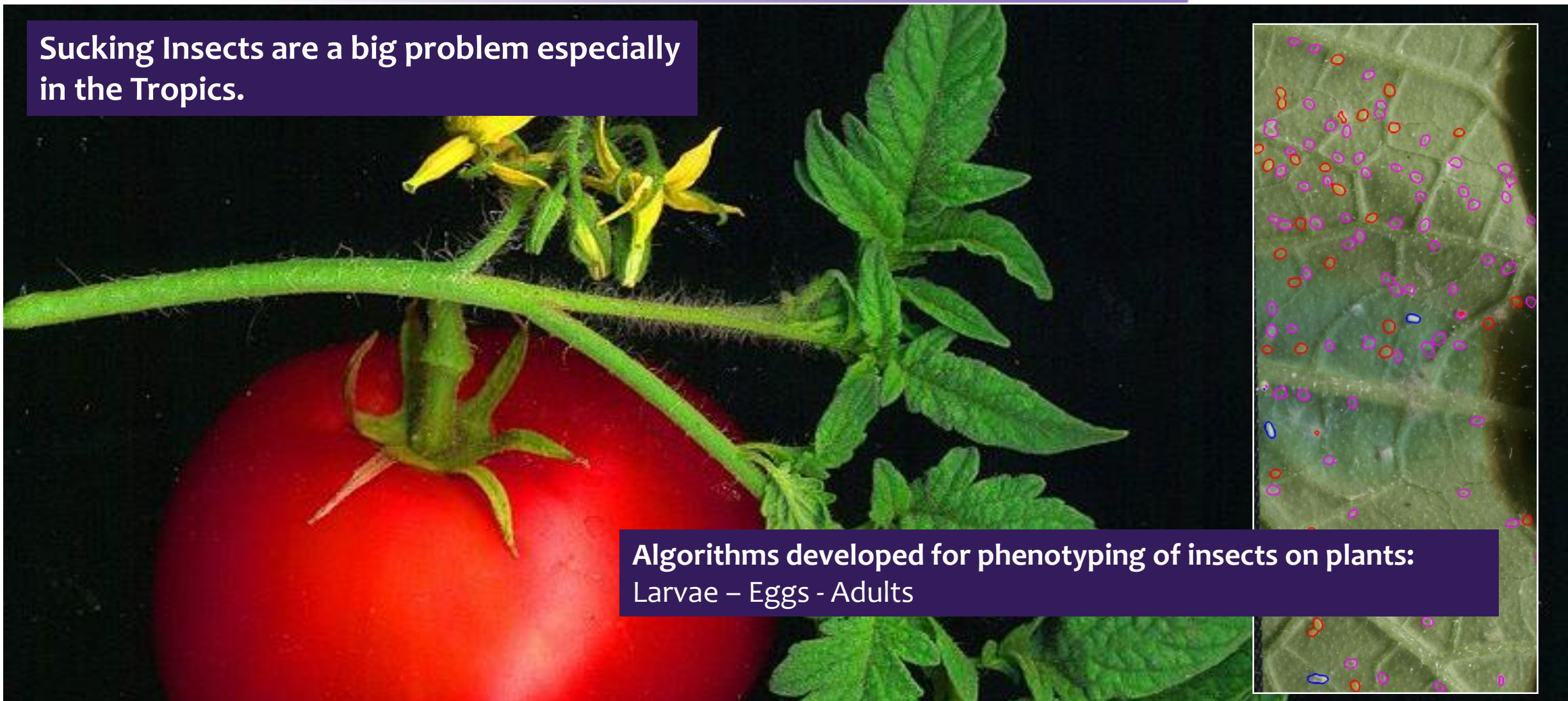


***Breakthrough Technologies
result in the development of
Better Traits in New and Improved Crops
in close collaboration
with partners all over the world***

Better Traits

Sucking Insect Resistance in tomato

Sucking Insects are a big problem especially in the Tropics.

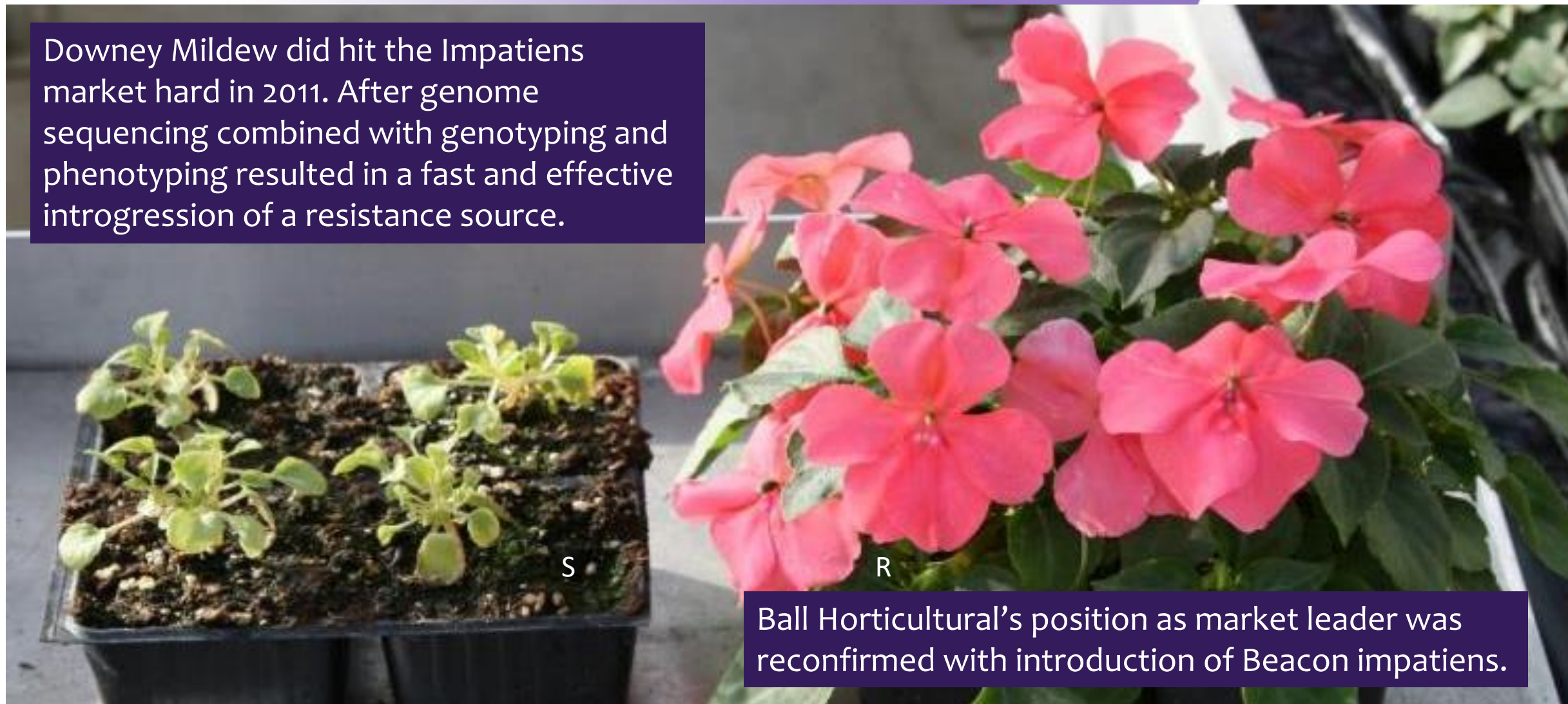


Algorithms developed for phenotyping of insects on plants:
Larvae – Eggs - Adults

Better Traits

Accelerated Resistance breeding in ornamentals

Downey Mildew did hit the Impatiens market hard in 2011. After genome sequencing combined with genotyping and phenotyping resulted in a fast and effective introgression of a resistance source.



Ball Horticultural's position as market leader was reconfirmed with introduction of Beacon impatiens.

Better Traits

Improved rice - Trials Italy, Po Delta 2016

KeyPoint® Breeding resulted in rice with a single base pair mutation that has higher yield and erect panicles



Rice is a main staple food all around the world including Europe where we have “Risotto” rice production in the Po delta.

Better Traits

Broad Virus Resistance in Crops

KeyPoint® Breeding resulted in virus resistant pepper and other crops with single base pair mutation

To be further announced at the MPMI conference in Glasgow, 14th July 2019 by Prof Marcel Prins, KeyGene

New and Improved Crops

Genomics & Phenomics enables development of new and improved crops

Improved Crops:

- Numerous vegetables, field crop and plantation crops

New Crops:

- Stevia for natural sweeteners
- Medicinal cannabis for cannabinoids
- Lupines for plant proteins
- Banana for bananas
- **Dandelion for natural rubber**



Banana flowering in Wageningen, Netherlands



Lupinus albus

New and Improved Crops

Breakthrough: sustainably produced natural rubber

Natural rubber remains essential in today's economy. The production is however exposed to threats, including price/supply volatility, diseases and environmental concern linked to SE Asia deforestation.



KeyGene used own genomics to develop the world first interspecies hybrid **Dandelion** variety “**Flexilis[®] hybrid**”. This novel agricultural crop enables annual rubber production in temperate climates.

Inuline as side product

Conclusions

Breakthrough Technologies result in the development of **Better Traits** in **New and Improved Crops** and vice-versa
New and Improved Crops and **Better Traits** require the development of **Breakthrough Technologies**
.... and this cycle goes on and on and on

*“Together with my KeyGene colleagues and all our partners
I am proud and thankful to be part of this Innovation Cycle
that helps our societies forward and will enable us to feed the world.”*

Arjen van Tunen, CEO KeyGene

Bedankt

Thank You



KeyGene®, KeyPoint®, KeySeeQ® PhenoFab® and Flexilis® are registered trademarks of Keygene N.V. in one or more territories in the world. The KeyPoint® Breeding technology is protected by patents and/or patent applications owned by Keygene N.V. All other products names, brand names or company names are used for identification purposes only, and may be (registered) trademarks of their respective owners.